Efficient Generation of Induced Pluripotent Stem and Neural Progenitor Cells From Acutely Harvested Dura Mater Obtained During Ventriculoperitoneal Shunt Surgery.

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Public Summary:
BACKGROUND: The dura mater can be easily biopsied during most cranial neurosurgical operations. We describe a protocol that allows for robust generation of induced pluripotent stem cells (iPSCs) and neural progenitors from acutely harvested dura mater. OBJECTIVE: To generate iPSCs and neural progenitor cells from dura mater obtained during ventriculoperitoneal shunt surgery. METHODS: Dura was obtained during ventriculoperitoneal shunt surgery for normal pressure hydrocephalus from a 60-year-old patient with severe cognitive impairment. Fibroblasts were isolated from the dural matrix and transduced with nonintegrating Sendai virus for iPSC induction. A subset of successfully generated iPSC clones underwent immunocytochemical analysis, teratoma assay, karyotyping, and targeted neural differentiation. RESULTS: Eleven iPSC clones were obtained from the transduction of an estimated 600,000 dural fibroblasts after 3 passages. Three clones underwent immunocytochemical analysis and were shown to express the transcription factors OCT-4, SOX2, and the embryonic cell markers SSEA-4, TRA-1-60, and Nanog. Two clones were tested for pluripotency and formed teratomas at the injection site in immunodeficient mice. Three clones underwent chromosomal analysis and were found to have a normal metaphase spread and karyotype. One clone underwent targeted neural differentiation and formed neural rosettes as well as TuJ1/SOX1-positive neural progenitor cells. CONCLUSIONS: IPSCs and neural progenitor cells can be efficiently derived from the dura of patients who need to undergo cranial neurosurgical operations. IPSCs were obtained with a nonintegrating virus and exhibited a normal karyotype, making them candidates for future autotransplantation after targeted differentiation to treat functional deficits.

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